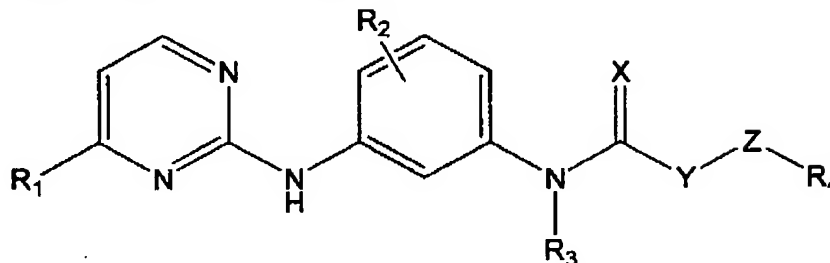


Application Number: 10/821,382

Clean amended claims

What is claimed is:

1. A phenylaminopyrimidine compound of formula (I)



Formula (I)

Wherein

X is oxygen or sulfur,

Y is a direct bond, oxygen, nitrogen or lower alkyl,

Z is an aliphatic, cycloaliphatic, aryl or a heterocyclyl radical,

R₁ is heterocyclyl radical,

R₂ is hydrogen, halogen, halogenlower alkyl, lower alkyl or lower alkoxy,

R₃ is hydrogen or lower alkyl,

R₄ is oxy-lower alkylamino, lower alkyl oxy-lower alkylamino, oxyheterocyclyl, lower alkyl oxyheterocyclyl, oxy-lower alkylheterocyclyl, lower alkyl oxy-lower alkylheterocyclyl, halogenlower alkylamino, halogenlower alkylheterocyclyl, lower alkylamino lower alkylamino,

aminoheterocyclyl with the proviso that heterocyclyl defined herein is not selected from N-lower alkylpyrrolidinyl or N-lower alky piperidinyl,

lower alkylamino heterocyclyl with the proviso that lower alkyamino defined herein is not para-substituted with -CH₂NH- when Z is the phenyl ring,

amino lower alkylheterocyclyl or lower alkylamino lower alkylheterocyclyl,

or a pharmaceutically acceptable salt thereof.

2. A compound of Formula (I) according to claim 1, wherein

X is oxygen or sulfur,

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Y is a direct bond, oxygen, nitrogen or lower alkyl,

Z is an aliphatic, cycloaliphatic, aryl or a heterocyclyl radical,

R₁ is heterocyclyl radical,

R₂ is hydrogen, halogen, halogenlower alkyl, lower alkyl or lower alkoxyl,

R₃ is hydrogen or lower alkyl,

R₄ is:

(a) oxy-lower alkyl unsubstituted, mono or disubstituted amino; oxy-lower alkyl morpholinyl, oxy-lower alkyl pyrrolidinyl, oxy-lower alkyl piperidinyl, oxy-lower alkyl piperazinyl, oxy-pyrrolidinyl, oxy-piperidinyl,

(b) lower alkyl oxy-lower alkyl unsubstituted, mono or disubstituted amino; lower alkyl oxy-lower alkyl morpholinyl, lower alkyl oxy-lower alkyl pyrrolidinyl, lower alkyl oxy-lower alkyl piperidinyl, lower alkyl oxy-lower alkyl piperazinyl, lower alkyl oxy-pyrrolidinyl, lower alkyl oxy-piperidinyl,

(c) mono or difluoro substituted lower alkyl unsubstituted, mono or disubstituted amino; mono or difluoro substituted lower alkyl morpholinyl, mono or difluoro substituted lower alkyl pyrrolidinyl, mono or difluoro substituted lower alkyl piperidinyl, mono or difluoro substituted lower alkyl piperazinyl,

(d) amino lower alkyl morpholinyl, amino lower alkyl pyrrolidinyl, amino lower alkyl piperidinyl, amino lower alkyl piperazinyl,

amino pyrrolidinyl, amino piperidinyl with the proviso that pyrrolidinyl or piperidinyl defined herein is not selected from N-lower alkylpyrrolidinyl or N-lower alkyl piperidinyl,

(e) lower alkylamino lower alkyl unsubstituted, mono or disubstituted amino; lower alkylamino lower alkyl morpholinyl, lower alkylamino lower alkyl pyrrolidinyl, lower alkylamino lower alkyl piperidinyl, lower alkylamino lower alkyl piperazinyl,

lower alkylamino heterocyclyl with the proviso that lower alkylamino defined herein is not para-substituted with $-\text{CH}_2\text{NH}-$ when Z is the phenyl ring,

or a pharmaceutically acceptable salt thereof.

3. A compound of Formula (I) according to claim 1, wherein

X is oxygen or sulfur,

Y is a direct bond,

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Z is an aliphatic, cycloaliphatic, aryl or a heterocyclyl radical,

R₁ is heterocyclyl radical,

R₂ is hydrogen, halogen, halogenlower alkyl, lower alkyl or lower alkoxyl,

R₃ is hydrogen or lower alkyl,

R₄ is:

(a) oxy-lower alkyl unsubstituted, mono or disubstituted amino; oxy-lower alkyl morpholinyl, oxy-lower alkyl pyrrolidinyl, oxy-lower alkyl piperidinyl, oxy-lower alkyl piperazinyl, oxy-pyrrolidinyl, oxy-piperidinyl,

(b) lower alkyl oxy-lower alkyl unsubstituted, mono or disubstituted amino; lower alkyl oxy-lower alkyl morpholinyl, lower alkyl oxy-lower alkyl pyrrolidinyl, lower alkyl oxy-lower alkyl piperidinyl, lower alkyl oxy-lower alkyl piperazinyl, lower alkyl oxy-pyrrolidinyl, lower alkyl oxy-piperidinyl,

(c) mono or difluoro substituted lower alkyl unsubstituted, mono or disubstituted amino; mono or difluoro substituted lower alkyl morpholinyl, mono or difluoro substituted lower alkyl pyrrolidinyl, mono or difluoro substituted lower alkyl piperidinyl, mono or difluoro substituted lower alkyl piperazinyl,

(d) amino lower alkyl morpholinyl, amino lower alkyl pyrrolidinyl, amino lower alkyl piperidinyl, amino lower alkyl piperazinyl,

amino pyrrolidinyl, amino piperidinyl with the proviso that pyrrolidinyl or piperidinyl defined herein is not selected from N-lower alkylpyrrolidinyl or N-lower alkyl piperidinyl,

(e) lower alkylamino lower alkyl unsubstituted, mono or disubstituted amino; lower alkylamino lower alkyl morpholinyl, lower alkylamino lower alkyl pyrrolidinyl, lower alkylamino lower alkyl piperidinyl, lower alkylamino lower alkyl piperazinyl,

lower alkylamino heterocyclyl with the proviso that lower alkylamino defined herein is not para-substituted with -CH₂NH- when Z is the phenyl ring,

or a pharmaceutically acceptable salt thereof.

4. A compound of Formula (I) according to claim 1, wherein

X is oxygen or sulfur,

Y is a direct bond,

Z is aryl,

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R₁ is heterocyclyl radical,

R₂ is hydrogen, halogen, halogenlower alkyl, lower alkyl or lower alkoxy,

R₃ is hydrogen or lower alkyl,

R₄ is:

(a) oxy-lower alkyl unsubstituted, mono or disubstituted amino; oxy-lower alkyl morpholinyl, oxy-lower alkyl pyrrolidinyl, oxy-lower alkyl piperidinyl, oxy-lower alkyl piperazinyl, oxy-pyrrolidinyl, oxy-piperidinyl,

(b) lower alkyl oxy-lower alkyl unsubstituted, mono or disubstituted amino; lower alkyl oxy-lower alkyl morpholinyl, lower alkyl oxy-lower alkyl pyrrolidinyl, lower alkyl oxy-lower alkyl piperidinyl, lower alkyl oxy-lower alkyl piperazinyl, lower alkyl oxy-pyrrolidinyl, lower alkyl oxy-piperidinyl,

(c) mono or difluoro substituted lower alkyl unsubstituted, mono or disubstituted amino; mono or difluoro substituted lower alkyl morpholinyl, mono or difluoro substituted lower alkyl pyrrolidinyl, mono or difluoro substituted lower alkyl piperidinyl, mono or difluoro substituted lower alkyl piperazinyl,

(d) amino lower alkyl morpholinyl, amino lower alkyl pyrrolidinyl, amino lower alkyl piperidinyl, amino lower alkyl piperazinyl,

amino pyrrolidinyl, amino piperidinyl with the proviso that pyrrolidinyl or piperidinyl defined herein is not selected from N-lower alkylpyrrolidinyl or N-lower alkyl piperidinyl,

(e) lower alkylamino lower alkyl unsubstituted, mono or disubstituted amino; lower alkylamino lower alkyl morpholinyl, lower alkylamino lower alkyl pyrrolidinyl, lower alkylamino lower alkyl piperidinyl, lower alkylamino lower alkyl piperazinyl,

lower alkylamino heterocyclyl with the proviso that lower alkylamino defined herein is not para-substituted with -CH₂NH- when Z is the phenyl ring,

or a pharmaceutically acceptable salt thereof.

5. A compound of Formula (I) according to claim 1, wherein

X is oxygen or sulfur,

Y is a direct bond,

Z is aryl,

R₁ is heterocyclyl radical,

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R₂ is halogenlower alkyl or lower alkyl,

R₃ is hydrogen or lower alkyl,

R₄ is:

(a) oxy-lower alkyl unsubstituted, mono or disubstituted amino; oxy-lower alkyl morpholinyl, oxy-lower alkyl pyrrolidinyl, oxy-lower alkyl piperidinyl, oxy-lower alkyl piperazinyl, oxy-pyrrolidinyl, oxy-piperidinyl,

(b) lower alkyl oxy-lower alkyl unsubstituted, mono or disubstituted amino; lower alkyl oxy-lower alkyl morpholinyl, lower alkyl oxy-lower alkyl pyrrolidinyl, lower alkyl oxy-lower alkyl piperidinyl, lower alkyl oxy-lower alkyl piperazinyl, lower alkyl oxy-pyrrolidinyl, lower alkyl oxy-piperidinyl,

(c) mono or difluoro substituted lower alkyl unsubstituted, mono or disubstituted amino; mono or difluoro substituted lower alkyl morpholinyl, mono or difluoro substituted lower alkyl pyrrolidinyl, mono or difluoro substituted lower alkyl piperidinyl, mono or difluoro substituted lower alkyl piperazinyl,

(d) amino lower alkyl morpholinyl, amino lower alkyl pyrrolidinyl, amino lower alkyl piperidinyl, amino lower alkyl piperazinyl,

amino pyrrolidinyl, amino piperidinyl with the proviso that pyrrolidinyl or piperidinyl defined herein is not selected from N-lower alkylpyrrolidinyl or N-lower alkyl piperidinyl,

(e) lower alkylamino lower alkyl unsubstituted, mono or disubstituted amino; lower alkylamino lower alkyl morpholinyl, lower alkylamino lower alkyl pyrrolidinyl, lower alkylamino lower alkyl piperidinyl, lower alkylamino lower alkyl piperazinyl,

lower alkylamino heterocyclyl with the proviso that lower alkyamino defined herein is not para-substituted with -CH₂NH- when Z is the phenyl ring, or a pharmaceutically acceptable salt thereof.

6. A compound of Formula (I) according to claim 1, wherein

X is oxygen or sulfur,

Y is a direct bond,

Z is aryl,

R₁ is heterocyclyl radical,

R₂ is lower alkyl,

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R₃ is hydrogen,

R₄ is:

(a) oxy-lower alkyl unsubstituted, mono or disubstituted amino; oxy-lower alkyl morpholinyl, oxy-lower alkyl pyrrolidinyl, oxy-lower alkyl piperidinyl, oxy-lower alkyl piperazinyl, oxy-pyrrolidinyl, oxy-piperidinyl,

(b) lower alkyl oxy-lower alkyl unsubstituted, mono or disubstituted amino; lower alkyl oxy-lower alkyl morpholinyl, lower alkyl oxy-lower alkyl pyrrolidinyl, lower alkyl oxy-lower alkyl piperidinyl, lower alkyl oxy-lower alkyl piperazinyl, lower alkyl oxy-pyrrolidinyl, lower alkyl oxy-piperidinyl,

(c) mono or difluoro substituted lower alkyl unsubstituted, mono or disubstituted amino; mono or difluoro substituted lower alkyl morpholinyl, mono or difluoro substituted lower alkyl pyrrolidinyl, mono or difluoro substituted lower alkyl piperidinyl, mono or difluoro substituted lower alkyl piperazinyl,

(d) amino lower alkyl morpholinyl, amino lower alkyl pyrrolidinyl, amino lower alkyl piperidinyl, amino lower alkyl piperazinyl,

amino pyrrolidinyl, amino piperidinyl with the proviso that pyrrolidinyl or piperidinyl defined herein is not selected from N-lower alkylpyrrolidinyl or N-lower alkyl piperidinyl,

(e) lower alkylamino lower alkyl unsubstituted, mono or disubstituted amino; lower alkylamino lower alkyl morpholinyl, lower alkylamino lower alkyl pyrrolidinyl, lower alkylamino lower alkyl piperidinyl, lower alkylamino lower alkyl piperazinyl,

lower alkylamino heterocyclyl with the proviso that lower alkylamino defined herein is not para-substituted with -CH₂NH- when Z is the phenyl ring,

or a pharmaceutically acceptable salt thereof.

7. A compound of Formula (I) according to claim 1, wherein

X is oxygen,

Y is a direct bond,

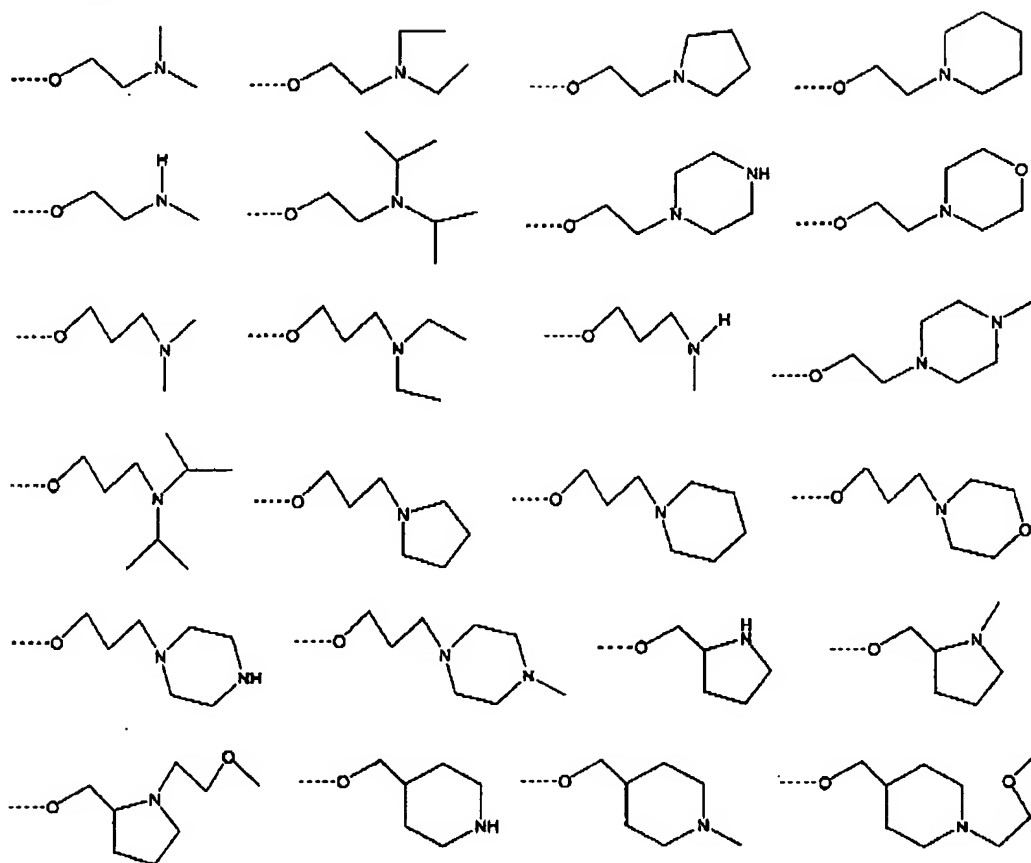
Z is phenyl,

R₁ is: 3-pyridyl or 4-pyridyl

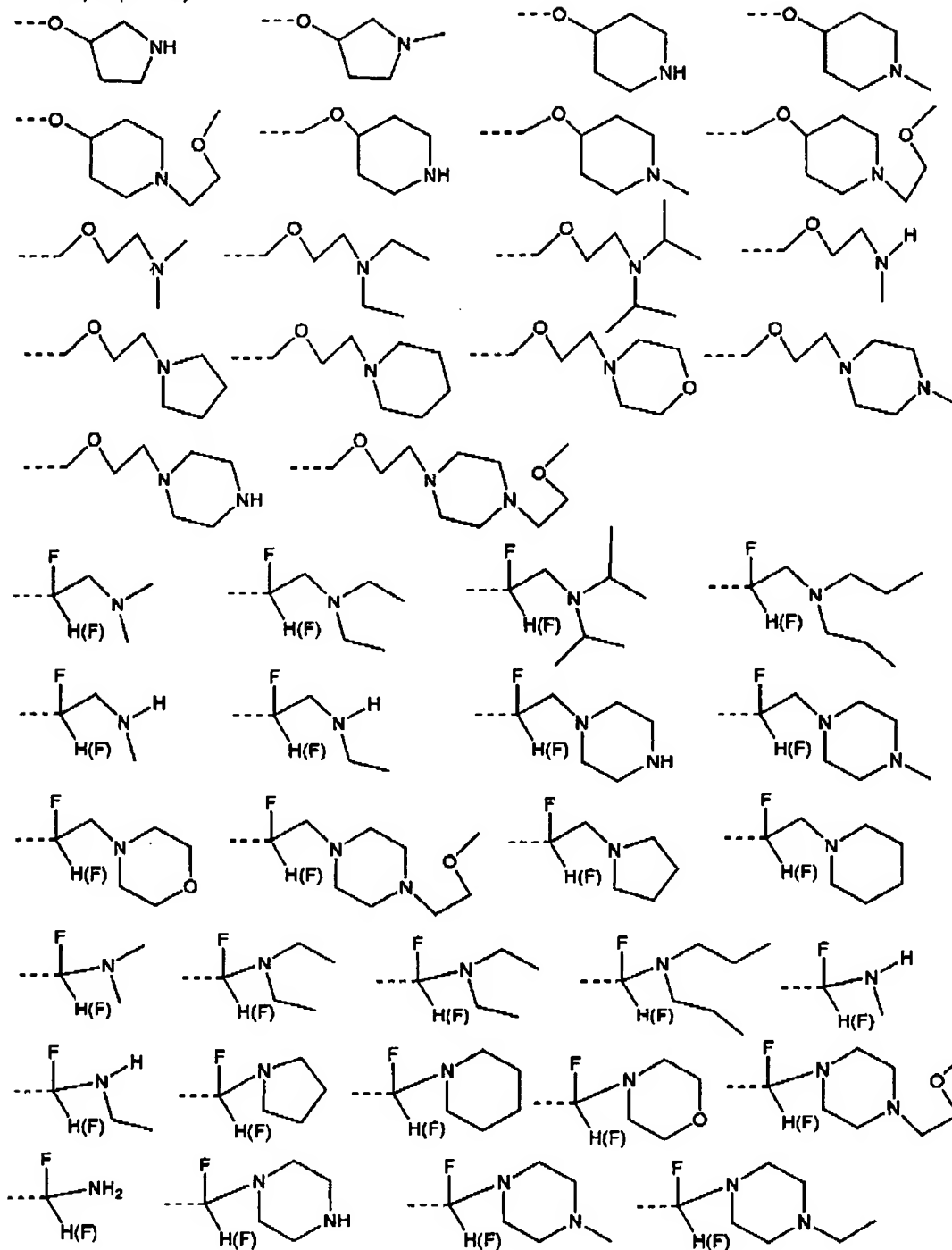
R₂ is: methyl, F, Cl or hydrogen,

R₃ is hydrogen,

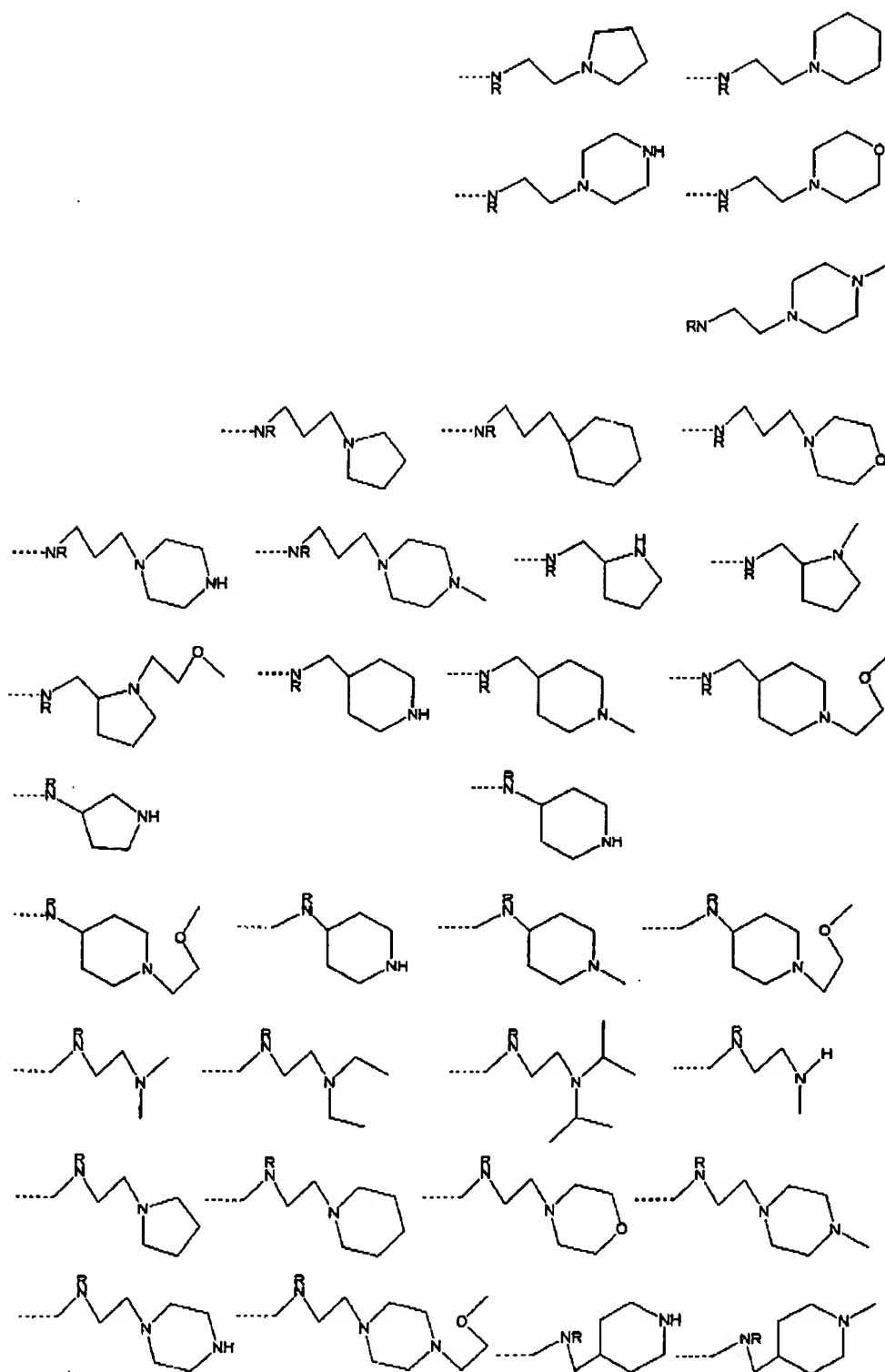
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R₄ is:

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 R_4 is (cont'd) :

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 R_4 is (cont'd) :

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R is hydrogen, lower alkyl, aliphatic, or cycloaliphatic-radicals,
or a pharmaceutically acceptable salt thereof.

8. A compound of Formula (I) according to claim 1 is selected from:

[4-(2-aminoethoxy)phenyl]-N-{4-methyl-3-[(4-(3-pyridyl)-pyrimidin-2-yl)amino]phenyl}carboxamide

[4-(fluoropiperazinylmethyl)phenyl]-N-{4-methyl-3-[(4-(3-pyridyl)-pyrimidin-2-yl)amino]phenyl}carboxamide

N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}-{4-[(1-methylpyrrolidin-2-yl)methoxy]phenyl}carboxamide

N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}[4-(pyrrolidin-3-ylamino)phenyl]carboxamide

[4-(aminofluoromethyl)phenyl]-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}[4-(methylpyrrolidin-3-ylamino)phenyl]carboxamide

{4-[fluoro(4-methylpiperazinyl)methyl]phenyl}-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

[4-(aminodifluoromethyl)phenyl]-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

(4-{fluoro[(1-methylpyrrolidin-3-yl)amino]methyl}phenyl)-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

{4-[fluoro(methylpyrrolidin-3-ylamino)methyl]phenyl}-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

[4-({[2-(dimethylamino)ethyl]amino}fluoromethyl)phenyl]-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

[4-(difluoropiperazinylmethyl)phenyl]-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

{4-[difluoro(4-methylpiperazinyl)methyl]phenyl}-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

[4-({[2-(dimethylamino)ethyl]amino}difluoromethyl)phenyl]-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

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(4-{fluoro[methyl(1-methylpyrrolidin-3-yl)amino]methyl}-phenyl)-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide
{4-[fluoro(pyrrolidin-3-ylamino)methyl]phenyl}-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide
{4-[(4-ethylpiperazinyl)difluoromethyl]phenyl}-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide
{4-[(4-ethylpiperazinyl)fluoromethyl]phenyl}-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide
(4-{difluoro[methyl(1-methylpyrrolidin-3-yl)amino]methyl}-phenyl)-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide
{4-[difluoro(methylpyrrolidin-3-ylamino)methyl]phenyl}-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide
[4-({[2-(dimethylamino)ethyl]amino}fluoromethyl)phenyl]-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide
{4-[difluoro(pyrrolidin-3-ylamino)methyl]phenyl}-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide
(4-{[methyl(1-methylpyrrolidin-3-yl)amino]methyl}phenyl)-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide
{4-(methylpyrrolidin-3-ylamino)methylphenyl}-N-{4-methyl-3-[(4-(3-pyridyl)pyrimidin-2-yl)amino]phenyl}carboxamide

or a pharmaceutically acceptable salt thereof.

9. A pharmaceutical acceptable salt according to any one of claims 1 to 8 is methanesulfonic acid salt.

10. A pharmaceutical composition which comprises as an active ingredient a compound as defined in any one of claims 1 to 8 or a pharmaceutical acceptable salt of the compound, or a hydrate or solvate of the compound and a pharmaceutical acceptable carrier.